

[HOME](#) [ABOUT IAC](#) [CONTACT](#) [A-Z INDEX](#) [DONATE](#) [SHOP](#) [SUBSCRIBE](#)

For Healthcare Professionals

For the Public

For Coalitions

Immunization Action Coalition

Sign up for email newsletter

Custom Search

Search

Favorites

Handouts & Staff Materials

Clinic Tools

Vaccine Information Statements

Vaccines

Talking about Vaccines

IAC Home | Ask the Experts | [Scheduling Vaccines](#)

Ask the Experts

Scheduling Vaccines

[Ask the Experts Home](#)

- [Administering Vaccines](#)
- [Billing and Reimbursement](#)
- [Combination Vaccines](#)
- [Diphtheria](#)
- [Documenting Vaccination](#)
- [Hib](#)
- [Hepatitis A](#)
- [Hepatitis B](#)
- [HPV](#)
- [Influenza](#)
- [MMR](#)
- [Meningococcal ACWY](#)
- [Meningococcal B](#)
- [Pertussis](#)
- [Pneumococcal](#)
- [Polio](#)
- [Precautions and Contraindications](#)
- [Rabies](#)
- [Rotavirus](#)
- [Scheduling Vaccines](#)
- [Storage and Handling](#)
- [Tetanus](#)
- [Travel Vaccines](#)
- [Vaccine Recommendations](#)
- [Vaccine Safety](#)
- [Varicella \(chickenpox\)](#)
- [Zoster \(shingles\)](#)

Scheduling Vaccines

Why are vaccines generally not given to infants younger than 6 weeks of age in the U.S.?

Mainly because little safety or efficacy data exist on doses given before 6 weeks of age, and the vaccines aren't licensed for this use. The data that exist suggest that the response to doses given before 6 weeks is poor and in some cases (such as Haemophilus influenzae type b vaccine) the response could be detrimental to the infant by possibly reducing the immune response to subsequent doses of Hib conjugate vaccine. Hepatitis B vaccine is an exception because infants respond adequately to this vaccine as early as the day of birth and early receipt of this vaccine is necessary to protect infants born to HBsAg-positive mothers.

Is it necessary to start a vaccine series over if a patient doesn't come back for a dose at the recommended time, even if there's been a year or more delay?

For routinely administered vaccines, there is no vaccine series that needs to be restarted because of an interval that is longer than recommended. In certain circumstances, oral typhoid vaccine (which may be given for international travel) needs to be restarted if the vaccine series isn't completed within the recommended time frame.

What is meant by "minimum intervals" between vaccine doses?

Vaccination schedules are generally determined by clinical trials, usually prior to licensure of the vaccine. The spacing of doses in the clinical trial usually becomes the recommended schedule. A "minimum interval" is shorter than the recommended interval between doses, and is the shortest time between two doses of a vaccine series in which an adequate response to the second dose can be expected. The concern is that a dose given too soon after the previous dose may reduce the response to that dose. The minimum spacing between doses is generally included in the ACIP recommendation for that vaccine which can be found at www.cdc.gov/vaccines/hcp/acip-recs/index.html. In addition, an extensive listing of recommended and minimum intervals and ages for vaccination can be found in the ACIP General Best Practices Guidelines for Immunization, available at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html#, Table 3-1.

In updating immunizations for immigration ("green card") exams, I regularly come across intervals between catch-up vaccine doses that are shorter than ACIP recommendations—most often the last 2 doses of IPV are given less than 6 months apart, but also sometimes the 2 doses of varicella are given less than 3 months apart, and the next-to-last and last Td are given less than 6 months apart. How significant is this in terms of immunity?

The significance of non-standard intervals probably depends on the vaccine and the dose. This is a complex issue—studies have not been done to examine the effect of various intervals between doses on the immunogenicity of those doses. But ACIP has examined the available data and made recommendations about the minimum acceptable interval between doses for that dose to be considered valid (there is no maximum interval between doses). These minimum intervals are published as Table 3-1 in ACIP's General Best Practice Guidelines on Immunization, available at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html. Doses with a minimum interval less than the recommended minimum, as described in Table 3-1, should not be counted as valid. More details on this topic can be found in the *General Best Practice Guidelines*.

How can we quickly determine how to "catch up" children who have fallen behind on their shots?

As a general rule, infants or children who are more than 1 month or 1 dose behind schedule should be on an accelerated schedule, which means the intervals between doses should be reduced to the minimum allowable. Catch-up schedules for children ages 4 months through 18 years are included with each year's recommended immunization schedule that is issued by ACIP, AAP, and American Academy of Family Physicians (AAFP). To obtain a copy, go to www.cdc.gov/vaccines/schedules/hcp/index.html.

When a 3-month-old infant presents having had no prior immunizations, would you start the accelerated schedule?

The accelerated schedule should be used when the child is more than a month behind schedule, until you get them caught up. An accelerated schedule is acceptable as long as minimum ages and minimum intervals are observed for each dose. Once you have the child back on schedule, use the recommended ages and intervals on the childhood schedule. In this case you can give the child the first set of recommended vaccines at age 3 months and then bring him back at age 4 months and give the second

set of vaccinations. At this point the child will be caught up and can return to the usual schedule. Be sure to educate the parents and talk to them about the importance of bringing the child back on time.

If a child falls behind on immunizations, is it recommended to use only minimum intervals to get the child caught up? Or should we use a minimum interval for the same vaccine only once?

If a child is behind on immunizations, the Advisory Committee on Immunization Practices (ACIP) recommends using the minimum intervals between each dose until the child is caught up. The minimum interval for a vaccine can be used as many times as necessary, until the child is back on schedule.

If two live virus vaccines are inadvertently given less than 4 weeks apart, what should be done?

Two or more injectable or nasally administered live vaccines not administered on the same day should be separated by at least 4 weeks to minimize the potential risk for interference. If two such vaccines are separated by less than 4 weeks, the second vaccine administered should not be counted and the dose should be repeated at least 4 weeks later. Alternatively, one can perform serologic testing to check for immunity, but this option may be more costly, may not be practical if multiple antigens are involved (such as measles, mumps and rubella), and may provide results that are difficult to interpret.

The oral vaccines Ty21a typhoid, cholera and rotavirus vaccines can be administered on the same day with or at any interval before or after other live vaccines (injectable or intranasal). However, oral cholera vaccine should be administered before Ty21a vaccine, and 8 hours should separate the oral cholera vaccine and the first dose of Ty21a.

We gave a dose of vaccine too soon after the previous dose. When can we give another (valid) dose?

If vaccines are given too close together, it can result in a less than optimal immune response. However, in most instances, a difference of a few days is unlikely to have a negative effect on immune response. With the exception of rabies vaccine, ACIP allows a grace period of 4 days (i.e., vaccine doses administered up to 4 days before the recommended minimum interval or age can be counted as valid). However, if a dose was administered 5 or more days earlier than the recommended minimum interval between doses, it is not valid and must be repeated. The repeat dose should be spaced after the invalid dose by the recommended minimum interval.

If the first dose in a series is given 5 days or more before the recommended minimum age, the dose should be repeated on or after the date when the child reaches at least the minimum age. If the vaccine is a live vaccine, ensuring that a minimum interval of 28 days has elapsed from the invalid dose is recommended. Avoid such errors by knowing the minimum intervals and ages for routinely given vaccines. You can look up such information in the ACIP General Best Practices Guidelines for Immunization, available at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html#, Table 3-1.

The 4-day "grace period" should not be used when scheduling future vaccination visits, and should not be applied to the 28-day interval between live parenteral vaccines not administered at the same visit. It should be used primarily when reviewing vaccination records (for example, when evaluating a vaccination record prior to entry to daycare or school).

Two live virus vaccines can be given on the same day. How do you define "day"?

The "same day" generally means at the same visit. This interval has not been precisely defined and probably will never be since it would be extremely difficult to study in order to develop an evidence-based recommendation. Immunization programs (and their computer systems) likely define this differently. It seems reasonable that if two vaccines were given on the same date then they would both be valid.

For the purpose of vaccine spacing, what constitutes a month: 28 days (4 weeks), 30 days, or 31 days?

For intervals of 3 months or less, you should use 28 days (4 weeks) as a "month." For intervals of 4 months or longer, you should consider a month a "calendar month": the interval from one calendar date to the next a month later. This is a convention that was introduced on the childhood schedule in 2002 and discussed in the paper "Evaluation of Invalid Vaccine Doses" (Stokley S, Maurice E, Smith PJ, et al. *American Journal of Preventive Medicine*, 2004; 26[1]: 34–40).

Does live oral cholera vaccine need to be administered at an interval from other live oral or injectable vaccines?

In general, no. According to ACIP's General Best Practice Guidelines for Immunization, concerns about spacing between doses of live vaccines not given at the same visit applies only to live injectable or intranasal vaccines. So, live oral cholera vaccine may be administered simultaneously with another vaccine, or at any interval before or after administration of another vaccine. An exception is that live oral cholera vaccine should be administered before live oral Ty21a typhoid vaccine, and 8 hours should separate the oral cholera vaccine and the first dose of Ty21a.

The package insert for VaxChora oral cholera vaccine states that effectiveness and safety have not been established for revaccination or for individuals with previous immunity. Does the CDC have any recommendations on revaccination or is one dose considered lifetime immunity at this time?

At this time, CDC does not have any recommendation related to revaccination with oral cholera vaccine. The duration of immunity following one dose is unknown. As more information becomes available, CDC will update its recommendations accordingly.

A 3-year-old who was otherwise on schedule received some of her 15-month vaccinations (MMR, DTaP, IPV) twice due to a change in health plans. Can these doses be counted toward kindergarten vaccinations?

Whether these doses count as part of the child's series depends on the intervals between these doses and the ones that preceded them. If the second MMR was separated from the previous one by at least 4 weeks, it can be counted as the second MMR. No additional doses are indicated. The 4th dose of IPV is

recommended after the 4th birthday. In this case, the child would need a fifth dose of IPV on or after her fourth birthday. The fifth dose of DTaP should not be given earlier than age 4 years. Assuming this dose of DTaP was the fifth the child received, it was given much too early and should not be counted. The DTaP should be repeated on or after the child's fourth birthday.

If I give a pneumococcal polysaccharide vaccine to my patient now, how long must I wait before giving the influenza or Td vaccine?

Influenza vaccine and Td (or Tdap) may be given at the same time or at any time before or after a dose of pneumococcal polysaccharide vaccine. The only time you have to wait is when two LIVE vaccines are not given at the same visit; then you need to wait at least 4 weeks to give the second live vaccine.

Why can live zoster vaccine (Zostavax, Merck) be given without a delay after receipt of a blood product but a delay of up to a year is recommended for varicella vaccine (Varivax, Merck)?

This difference is due to the larger amount of varicella vaccine virus in live zoster vaccine. In the live zoster vaccine clinical trials all the participants had had varicella and were immune. So their pre-existing immunity (and the amount of antibody expected to be in most blood products) did not blunt their response to the vaccine. Varicella vaccine has a lower dose of varicella virus and is given to susceptible people. Passively-acquired antibody may interfere with the response to low-dose varicella vaccine for up to a year depending on what product is given.

What interval should be observed between receipt of a blood product and vaccination with live attenuated influenza vaccine (LAIV; FluMist, AstraZeneca)?

LAIV can be administered at any time before or after receipt of a blood product. See www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html#, Table 3-4, footnote B.

Do any of the bacterial vaccines that are recommended for people with functional or anatomic asplenia need to be given before splenectomy? Do the doses count if they are given during the 2 weeks prior to surgery?

Pneumococcal conjugate vaccine (PCV13, Prevnar 13, Pfizer), *Haemophilus influenzae* type b vaccine (Hib), meningococcal conjugate vaccine (MenACWY), and meningococcal B vaccine should be given 14 days before splenectomy, if possible. Doses given during the 2 weeks (14 days) before surgery can be counted as valid. If the doses cannot be given prior to the splenectomy, they should be given as soon as the patient's condition has stabilized after surgery. Pneumococcal polysaccharide vaccine (PPSV23, Pneumovax, Merck) should be administered 8 weeks after the dose of PCV13 for people 2 years of age and older.

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- Guide to immunize.org -

A-Z INDEX

ABOUT IAC

ACIP RECOMMENDATIONS

ADDITIONAL RESOURCES

ADULT VACCINATION

ADULT VACCINATION GUIDE

ASK THE EXPERTS

Combination Vaccines

Diphtheria

Hepatitis A

Hepatitis B

Vaccine Storage and Handling

>> view all

BECKY PAYNE AWARD

BILLING & CODING

BIRTH DOSE GUIDEBOOK

CALENDAR OF EVENTS

CDC INFORMATION

CDC SCHEDULES

CLINIC TOOLS

Administering Vaccines

Adult Vaccination

Documenting Vaccination

Scheduling Vaccination

Screening for Contraindications

Storage & Handling

DEAR COLLEAGUE LETTER HPV VACCINE

DEAR COLLEAGUE LETTER MCV4 DOSE #2

DISEASES & VACCINES

Diphtheria

Hepatitis A

Hepatitis B

Influenza

Varicella

>> view all

DONATE TO IAC

EMAIL NEWS SERVICES

EDUCATIONAL MATERIALS

EXEMPTIONS

FAQs

FAVORITES (WEB SECTIONS)

FDA PRODUCT APPROVALS

GIVE BIRTH TO THE END OF HEP B

HANDOUTS FOR PATIENTS & STAFF

Administering Vaccines

Adult Vaccination

Documenting Vaccinations

Managing Vaccine Reactions

Parent Handouts

Patient Schedules

Questions & Answers

HEPATITIS B BIRTH DOSE

HONOR ROLLS

HepB Birth Dose

Influenza Vaccination for HCP

IAC EARLY YEARS VIDEO

IAC EXPRESS

IMAGES

IMMUNIZATION TECHNIQUES DVD

LAMINATED SCHEDULES

LAWS AND MANDATES

MANUFACTURERS

NATIONAL ADULT & INFLUENZA IMMUNIZATION SUMMIT

NEWS & INFORMATION

OFFICIAL RELEASES

ACIP

CDC

FDA

>> view all

PACKAGE INSERTS

PARTNERS

PAYNE AWARD

PHARMACISTS

PRESS ROOM

PROTECT NEWBORNS FROM HEP B

PUBLICATIONS

IAC Express

Vaccinating Adults:
A Step-by-Step Guide

REGISTRIES

RESOURCE DIRECTORY

SHOP IAC

Immunization Techniques DVD

Laminated Schedules

Patient Record Cards

>> view all

SITE MAP

SLIDE SETS

STANDING ORDERS TEMPLATES

STATE INFORMATION

State Websites

State Laws

State Immunization Managers

>> view all

SUBSCRIBE

SUPPORT IAC

TECHNICALLY SPEAKING

TIMELINE FOR VACCINES

UNPROTECTED PEOPLE REPORTS

Chickenpox

Diphtheria

Hepatitis A

Hepatitis B

>> view all

VACCINATING ADULTS: A STEP-BY- STEP GUIDE

VACCINE CONCERNS

Adjuvants & Ingredients

Alternative Medicine

Autism

Importance of Vaccination

>> view all

VACCINE INFORMATION STATEMENTS

Translations

Vaccine Index

>> view all

VACCINE MANUFACTURERS

VACCINE POLICY & LICENSURE

ACIP

FDA

WHO

>> view all

VACCINE SAFETY

VACCINE TIMELINE

VACCINES & DISEASES

VIDEO ABOUT IAC EARLY YEARS

[Vaccine Recommendations](#)[>> view all](#)[COALITIONS](#)[CONTRIBUTE TO IAC](#)[Recommendations](#)[Screening Checklists](#)[Standing Orders](#)[Storage & Handling](#)[Talking with Parents](#)[Temperature Logs](#)[Top Handouts](#)[Translations](#)[Vaccine Index](#)[>> view all](#)[PHOTOS](#)[POWERPOINT SLIDE SETS](#)[TRANSLATE FOR IAC](#)[TRANSLATIONS OF VISs](#)[TRAVEL \(INTERNATIONAL\)](#)[VIDEOS \(VIDEO OF THE WEEK\)](#)[WHAT'S NEW OR UPDATED AT IAC](#)[Handouts](#)[VISs and Translations](#)[Web Sections](#)[>> view all](#)[Home](#) • [About IAC](#) • [Contact Us](#) • [Donate](#) • [Press Room](#) • [Cite IAC](#) • [Link to IAC](#) • [A-Z Index](#) • [Site Map](#) • [Disclaimer](#) • [Content Review](#) • [Privacy Policy](#)

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